the framework is flexible enough to capture treatment effects that vary by line of therapy, and we demonstrate how appropriate discounting to allow for differential timing can still be made. We believe that the framework illustrated in this paper has wide applicability to sequencing models in many disease areas, most notably oncology and rheumatology where such sequencing models are common. We demonstrate the flexibility of the approach and show how time dependency can be incorporated at any sequence of the model without having to resort to individual patient simulation.

PRM139

A COMPREHENSIVE ECONOMIC AND PRICING MODELING FRAMEWORK FOR UNDERSTANDING ORPHAN DRUG DEVELOPMENT

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Rare diseases provide a perplexing problem for reimbursement agencies. Orphan drug development is often incentivized by government entities. Despite these incentives, reimbursement at a viable level is not assured, and recent efforts by reimbursement bodies are changing the reimbursement paradigm substantially. Value-based pricing agreements, which link the price of the drug to the value achieved, is one such effort. However, demonstrating value for an orphan drug remains challenging. To better understand the potential value and therefore pricing of orphan drugs, we developed a comprehensive model to evaluate the pricing, economics, reimbursement, and market strategy (PERMS) specifically for these drugs. The interactive simulation model was developed to combine evidence on development costs, cost-effectiveness, treatment pathways, improvements in quality of life, and market share. The PERMS model was designed to evolve alongside the drug development process, incorporating new parameters and data as they become known. Extensive sensitivity analyses are performed to highlight the substantial uncertainty in disease prevalence and costs of the diseases. An interactive interface is developed for users to examine how changes in model input values affect outcomes of interest. In this presentation, we will describe the primary elements of the PERMS model, demonstrate how the results may vary across subpopulations and illustrate the potential value of new drugs. Concepts will be illustrated through the use of real-world examples such as graft-versus-host disease (GVHD); a major complication of stem cell or bone marrow transplantation that has significant prognostic implications in the setting of a rare resource. This presentation will illustrate how a holistic view through simulation modeling can be useful and informative for understanding disease burden and potential reimbursement levels and making a decision to proceed to the next phase of drug development.

PRM140

CONCEPTUAL MODEL DEVELOPMENT AND PROS FOR NON-DIABETIC PERIPHERAL NEUROPATHIC PAIN

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OBJECTIVES: To demonstrate how a conceptual model of symptoms of non-diabetic peripheral neuropathic pain, impact on quality of life and tolerability of treatments helps to select patient reported outcomes (PROs) in clinical trials. To show that the selected PROs measure what is expected. **METHODS:** A literature review and interviews with 4 clinical experts were conducted to identify the PRO measurement concepts related to symptoms and impacts of highest importance and relevance to non-diabetic peripheral neuropathic pain patients. The mechanism of action of treatments available and in development were also included in the conceptual model. Based on this information, available instruments were evaluated to assess if measures focusing on emerging, central concepts were available and of relevance to a planned Phase IV study. **RESULTS:** Based on the literature review and expert interviews, pain was the predominant symptom concept. The most predominant impact concepts were difficulty with sleep quantity and quality. Available treatments suggested detrimental impact on cognition and local treatment-related pain. Instruments that seem to measure the central concepts were numerical pain rating scale scale (NPRS), MOS-Sleep and MOS-Cog. Furthermore the Treatment Satisfaction Questionnaire for Medication (TSQM) was assessed in order to be able to measure treatment satisfaction comparing different medications Results of the chosen PROs included in a Phase IV study with patients with non-diabetic peripheral neuropathic pain seem to show that they are able to measure the concepts they were selected to assess. **CONCLUSIONS:** The FDA PRO Guidance states that measures should be conceptually valid as they relate to the disease being studied, meet a threshold of psychometric soundness, and be relevant to patients. This research represents an important step toward establishing the PROs that could be used in studies with patients with non-diabetic peripheral neuropathic pain.

PRM141

MODELING ALL-CAUSE MORTALITY IN HEALTH ECONOMIC MODELS

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The estimation of life-years is an important component of many health economic models and this outcome is often required by health technology assessment agencies in the evaluation of health care technologies. Life-years are often obtained by adjusting the country-, age-, and gender-specific all-cause mortality, which considers all deaths in a population regardless of the cause, to account for additional deaths due to a specific disease (i.e., the disease-specific mortality). Properly modeling all-cause mortality and knowing the uncertainty associated with the estimates (if estimated) is therefore an important step in building a health economic model. The report of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Modeling Good Research Practices Task Force recommends modeling all-cause mortality non-parametrically based on life table data. This method uses the life table data directly to derive an empiric distribution of death times. Additionally, parametric survival analysis may be used to fit life table data. This method may be more flexible, avoiding the need to look up mortality hazards directly from life tables, requiring fewer parameters, and possibly saving computation time. Typically, this method is carried out by linearizing specific parametric survival distributions and using regression analysis on data from the life table to obtain estimates for the parameters of the distribution. Although this type of analysis is fairly straightforward, the estimates of the uncertainty around the parameters are inaccurate. A new method of obtaining these parameters, which involves simulating individual death times from the life table data and using maximum likelihood estimation to obtain the needed parameters, may be considered when modeling all-cause mortality. Utilizing the number of individuals at risk, this method may provide more accurate estimates of parameters and their uncertainty. The implementation, appropriateness, challenges, advantages and disadvantages of these three techniques when modeling all-cause mortality in health economic models will be discussed.

PRM142

JOINT BAYESIAN NETWORK META-ANALYSIS FOR EVENT COUNTS AND HAZARDS – COMPARISON OF METHODS AND IMPLEMENTATIONS

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Networks of treatments summarize all available information about the relative effectiveness of several treatments, also if both direct and indirect evidence needs to be combined[1]. For clinical trials with survival results, some will have been reported based on numbers of patients with event, and some based on the hazard ratio. A common scale for mapping the observed effects has been proposed[2]. Treatment contrasts would then be estimated through Bayesian methodology based on Markov Chain Monte Carlo (MCMC) simulation. Similar problems arise for trials with binary outcome. We investigate one example from pulmology and compare two implementations of the MCMC method, WinBUGS and SAS® PROC MCMC. Moreover, we investigate a deterministic-numerical approximation to the distribution of treatment contrasts, the integrated nested Laplace approximation (INLA) method. Of particular interest here is the goodness of the approximation, as the example dataset includes only small numbers of trials, patients and events. We show how to condense graphically the complex pattern of multiple treatment comparisons. We conclude with remarks on model selection, goodness-of-fit and the Deviance Information Criterion (DIC).

PRM143

PRACTICAL ISSUES WHEN CONDUCTING NETWORK META-ANALYSES WITH A LIMITED NUMBER OF STUDIES

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OBJECTIVES: Meta-analysis is being conducted extensively in part due to requirements from health care decision-making agencies. Meta-analysis techniques continue to develop, and software now exists to model networks using Bayesian or frequentist approaches with study effects treated as fixed or random. The non-model based anchored indirect-treatment comparison (AIC) method is also suitable for making pairwise treatment comparisons. However, practical issues emerge particularly when the network is comprised of a limited number of studies. Of special interest is the situation where a star network contains only one trial for a given treatment comparison. Our goal was to investigate the performance and interpretation of different meta-analysis methods when few studies are available. **METHODS:** Example star networks anchored by placebo were created for binary endpoints with varying proportions and sample sizes. Generalized linear mixed models were fitted using PROC GLIMMIX in SAS with a random study effect. Results were compared to the AIC method as well as analogous Bayesian models using WinBUGS. **RESULTS:** Estimated odds ratios were examined to identify patterns among methods. If placebo effects were largely different across individual trials, differences between methods varied depending on effect sizes and sample sizes. If placebo effects were similar, the frequentist random-effects model was not able to estimate a random study effect and it was reduced to a fixed-effect model (similar to the AIC). **CONCLUSIONS:** The limitations of conducting a meta-analysis with a small number of trials should be understood regardless of the methodology used. In the special case of a star network with only one trial per treatment comparison, the differences between methods depend on the underlying evidence. The implications for interpretation will be discussed.

PRM144

EXPLORING THE IMPACT OF STRUCTURAL UNCERTAINTY IN PARTITIONED SURVIVAL MODELS FOR ONCOLOGY

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OBJECTIVES: Economic evaluations in oncology built using partitioned survival analysis do not permit analysis of the post-progression period separately from the progression-free period. Moreover, when the outcomes are not complete at the time of the analysis, the benefits experienced by patients in the clinical trial used to inform the model are assumed to continue for the duration of the model due to extrapolation of the trial data using one set of parametric curves. The objective of this study is to present and contrast possible methods to address the structural uncertainty in the incremental effects and the cost-effectiveness estimates derived from partitioned survival models. **METHODS:** Options for addressing the long-term benefits in partitioned survival models are explored using a hypothetical economic model with three states (progression-free, progressed disease, and death). The methods include the standard approach of projecting treatment group PFS and OS outcomes using parametric survival curves, using time-varying hazard ratios to modify the relative benefits between treatments, calculating and modifying treatment-related Markov probabilities following progression in the cohort,